ABSTRACT OF THE DISCLOSURE

AAV Rep78 mutants comprising a modified AAV Rep78 protein that possesses different biochemical and biological functions as compared to the wild-type AAV Rep78 protein are disclosed. Particularly, the AAV Rep78 mutants that bind to at least one of a papillomavirus DNA or an AAV DNA or an oncogene or HIV DNA differently as compared to the wild-type AAV Rep78 protein, assays to select such mutants, and pharmaceutical compositions containing the AAV Rep78 mutants are disclosed. The present invention further discloses DNA sequences encoding at least one AAV Rep78 mutant that possesses different biochemical and biological functions as compared to the wild-type AAV Rep78 protein and pharmaceutical compositions comprising the DNA sequences. The present invention additionally is directed to a method of inhibiting papillomavirus associated diseases comprising administering pharmaceutical compositions containing AAV Rep78 mutants or the DNA sequences encoding the mutants. Also discloses are DNA sequences comprising the full length AAV genome modified to where the AAV Rep78 protein is replaced with an AAV Rep mutant that binds weakly or not at all to a papillomavirus DNA or an AAV DNA or both differently as compared to the wild-type AAV Rep78 protein and its use in producing recombinant AAV at increased levels production over wild-type levels of production. Further disclosed is a method of inhibiting papillomavirus-associated diseases, cancer, and HIV-associated diseases comprising administering a pharmaceutical composition comprising a wild-type AAV Rep78 or a mutant thereof to a patient afflicted with a papillomavirus-associated disease, cancer, or HIV-associated diseases. Particularly, useful in treating papillomavirus-assoicated diseases are the AAV Rep78 or mutant thereof that binds to nucleotides 14-56 of p97 of HPV-16 and inhibits expression of HPV oncoproteins. An AAV Rep78 regulation element of a DNA sequence comprising about nucleotides 14 –56 of the nucleotide sequence of Figure 2 and an AAV Rep78 regulatable promoter comprising the regulation element and a promoter sequence except for the HPV-16 p97 promoter.